language should read: (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), amino,

A clean copy of the claims as corrected is attached to this response.

Applicants thank the Examiner for the observations on the claims before commencement of examination on the merits, and request an early consideration of the claims directed to Group 2.

Respectfully submitted,

J. Mark Hoch

Date: 29 OCT 01

SIGNATURE OF PRACTITIONER

Registration no. 35195
Tel. no. 650-616-5035
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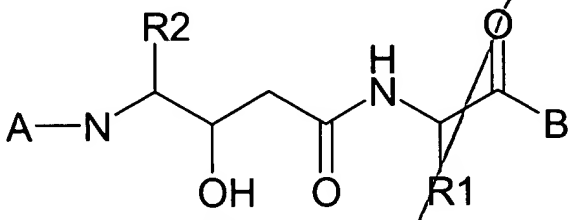
Customer no. 21835

J. Mark Hoch

Elan Pharmaceuticals, Inc.
800 Gateway Boulevard
South San Francisco, CA
94080

Clean copy of claims corrected in this response:

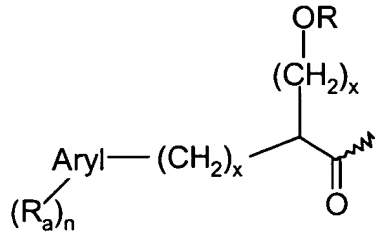
1) A compound of formula 1



Formula 1

wherein:
A is

i)



wherein Aryl is mono or bicyclic and has from 5 to 10 ring atoms and may optionally include up to 3 heteroatoms chosen from N, O and S;

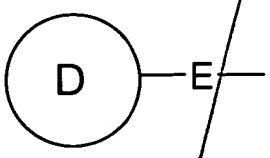
each x is independently 0, 1 or 2;

R is H, C_1-C_6 alkyl, phenyl or benzyl wherein each phenyl ring is optionally substituted with up to two groups independently selected from -OH; -CH_2OH, -CO_2H, -CF_3, Cl, Br, F; and C_1-C_2 alkyl;

each R_a is independently selected from the group consisting of H, OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy and N-heterocyclylacyl;

and n is 1 or 2;

ii)



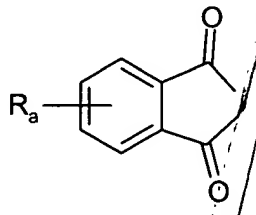
wherein D is chosen from aryl having 5 to 6 atoms, optionally including up to 2 heteroatoms selected from the N, O, and S; fused aryl of 8 to 14 atoms optionally including up to 3 heteroatoms selected from the N, O, and S; mono or fused cycloalkyl having 5 to 12 carbon atoms; and mono or fused heterocycloalkyl having 5 to 12 carbon atoms including up to 3 heteroatoms selected from N, O, and S; biaryl, diaryl ether; diarylketone, and phenyl(C_1-C_8) alkyloxyaryl;

and wherein E is a divalent group chosen from carbonyl, sulfonyl, C_1-C_3 alkylene, -X- (C_1-C_3) alkylcarbonyl wherein X is chosen from N, O and S, or E is merely a bond;

and D may optionally be substituted with up to two groups chosen from OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy, N-heterocyclylacyl, C_1-C_3 alkylsulfonyl, sulfonamide and C_1-C_3 alkylsulfonamide;

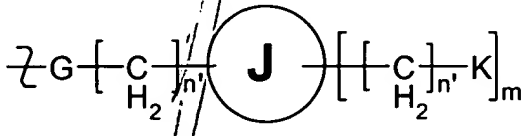
iii) C_1-C_6 alkanoyl; C_2-C_6 alkenoyl; and methylthioC_1-C_5 alkanoyl, any of which may be substituted with up to two groups chosen from OH, C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy; C_1-C_6 alkyloxy; C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), amino, C_1-C_6 alkyl and phenyl amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy and N-heterocyclylacyl, C_1-C_3 alkylsulfonyl, sulfonamide and C_1-C_3 alkylsulfonamide;

and iv) a divalent group of the formula:



wherein each carbonyl of the divalent group bonds to the nitrogen to form a five membered ring and Ra is as defined above;

B is selected from -OH; C_1-C_6 alkyl or C_1-C_6 alkyl amino, di(C_1-C_6 alkyl)amino, C_1-C_6 alkyloxy, N-heterocyclylic and



each n' is independently 0, 1 or 2;

m is 0, 1, 2 or 3;

and G is N or O;

J is selected from the group consisting of aryl having a 5 to 6 membered ring optionally including up to 2 heteroatoms selected from the N, O, and S; fused aryl rings of 8 to 14 atoms optionally including up to 3 heteroatoms selected from N, O, and S, mono or fused ring cycloalkyl having 5 to 12 carbon atoms; and mono or fused ring heterocyclic having 5 to 12 carbon atoms including up to 3 heteroatoms chosen from the group consisting of N, O, and S;

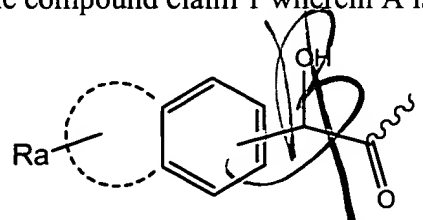
each K is chosen from OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters) and carboxy(C_2-C_5)alkyloxy;

R1 is straight or branched chain C_1-C_5 alkanyl or C_2-C_5 alkenyl;

R2 is C_{1-5} straight or branched chain alkanyl or alkenyl; methylthiomethyl; aryl or arylalkyl or heteroaryl or heteroarylalkyl wherein any of the above are optionally substituted with up to 2 of C_{1-3} alkyl, trifluoromethyl or halogen,

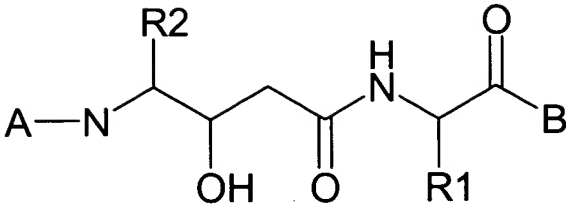
and stereoisomers, hydrates or pharmaceutically acceptable salts thereof.

2) The compound claim 1 wherein A is:



wherein the dotted line indicates an optional aryl ring fused to the phenyl ring.

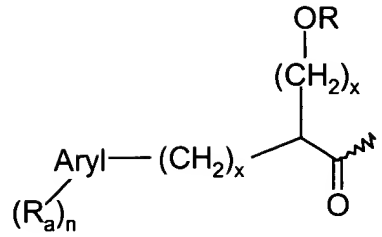
24) A method of slowing or ameliorating the progression of a disease state characterized by deposition of Aβ peptide in a mammal comprising administering to a mammal in need thereof an effective amount of a compound of formula 1



Formula 1

wherein:
A is

i)



wherein Aryl is mono or bicyclic and has from 5 to 10 ring atoms and may optionally include up to 3 heteroatoms chosen from N, O and S;

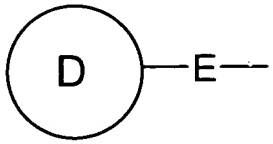
each x is independently 0, 1 or 2;

R is H, C_1-C_6 alkyl, phenyl or benzyl wherein each phenyl ring is optionally substituted with up to two groups independently selected from -OH; -CH_2OH, -CO_2H, -CF_3, Cl, Br, F; and C_1-C_2 alkyl;

each R_a is independently selected from the group consisting of H, OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy and N-heterocyclylacyl;

and n is 1 or 2;

ii)



wherein D is chosen from aryl having 5 to 6 atoms, optionally including up to 2 heteroatoms selected from the N, O, and S; fused aryl of 8 to 14 atoms optionally including up to

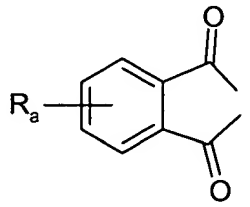
3 heteroatoms selected from the N, O, and S; mono or fused cycloalkyl having 5 to 12 carbon atoms; and mono or fused heterocycloalkyl having 5 to 12 carbon atoms including up to 3 heteroatoms selected from N, O, and S; biaryl, diaryl ether; diarylketone, and phenyl(C_1-C_8) alkyloxyaryl;

and wherein E is a divalent group chosen from carbonyl, sulfonyl, C_1-C_3 alkylene, -X- (C_1-C_3) alkylcarbonyl wherein X is chosen from N, O and S, or E is merely a bond;

and D may optionally be substituted with up to two groups chosen from OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy, N-heterocyclylacyl, C_1-C_3 alkylsulfonyl, sulfonamide and C_1-C_3 alkylsulfonamide;

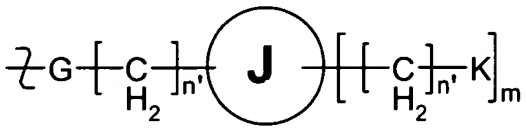
iii) C_1-C_6 alkanoyl; C_2-C-$_6$ alkenoyl; and methylthioC_1-C_5 alkanoyl, any of which may be substituted with up to two groups chosen from OH, C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy; C_1-C_6 alkyloxy; C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), amino, C_1-C_6 alkyl and phenyl amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy and N-heterocyclylacyl, C_1-C_3 alkylsulfonyl, sulfonamide and C_1-C_3 alkylsulfonamide;

and iv) a divalent group of the formula:



wherein each carbonyl of the divalent group bonds to the nitrogen to form a five membered ring and Ra is as defined above;

B is selected from -OH; C_1-C_6 alkyl or C_1-C_6 alkyl amino, di(C_1-C_6 alkyl)amino, C_1-C_6 alkyloxy, N-heterocyclylic and



each n' is independently 0, 1 or 2;

m is 0, 1, 2 or 3;

and G is N or O;

J is selected from the group consisting of aryl having a 5 to 6 membered ring optionally including up to 2 heteroatoms selected from the N, O, and S; fused aryl rings of 8 to 14 atoms optionally including up to 3 heteroatoms selected from N, O, and S, mono or fused ring cycloalkyl having 5 to 12 carbon atoms; and mono or fused ring heterocyclic having 5 to 12 carbon atoms including up to 3 heteroatoms chosen from the group consisting of N, O, and S;

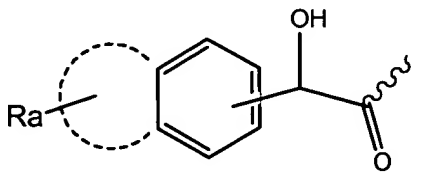
each K is chosen from OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters) and carboxy(C_2-C_5)alkyloxy;

R1 is straight or branched chain C_1-C_5 alkanyl or C_2-C_5 alkenyl;

R2 is C_{1-5} straight or branched chain alkanyl or alkenyl; methylthiomethyl; aryl or arylalkyl or heteroaryl or heteroarylalkyl wherein any of the above are optionally substituted with up to 2 of C_{1-3} alkyl, trifluoromethyl or halogen,

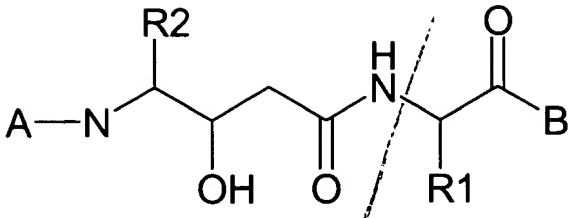
and pharmaceutically acceptable salts and esters thereof.

25) The method claim 24 wherein A is:



wherein the dotted line indicates an optional aryl ring fused to the phenyl ring.

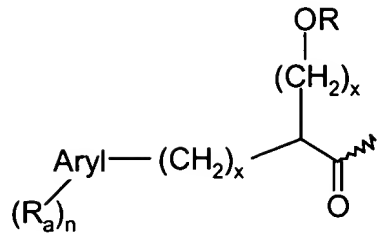
(47) A pharmaceutical composition comprising a compound of formula 1



Formula 1

wherein:
A is

i)



wherein Aryl is mono or bicyclic and has from 5 to 10 ring atoms and may optionally include up to 3 heteroatoms chosen from N, O and S;

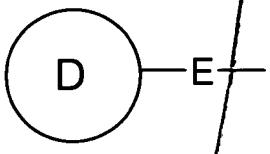
each x is independently 0, 1 or 2;

R is H, C_1-C_6 alkyl, phenyl or benzyl wherein each phenyl ring is optionally substituted with up to two groups independently selected from -OH; -CH_2OH, -CO_2H, -CF_3, Cl, Br, F; and C_1-C_2 alkyl;

each R_a is independently selected from the group consisting of H, OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy and N-heterocyclylacyl;

and n is 1 or 2;

ii)



wherein D is chosen from aryl having 5 to 6 atoms, optionally including up to 2 heteroatoms selected from the N, O, and S; fused aryl of 8 to 14 atoms optionally including up to

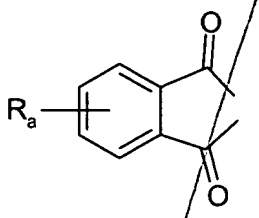
3 heteroatoms selected from the N, O, and S; mono or fused cycloalkyl having 5 to 12 carbon atoms; and mono or fused heterocycloalkyl having 5 to 12 carbon atoms including up to 3 heteroatoms selected from N, O, and S; biaryl, diaryl ether; diarylketone, and phenyl(C_1-C_8) alkyloxyaryl;

and wherein E is a divalent group chosen from carbonyl, sulfonyl, C_1-C_3 alkylene, -X- (C_1-C_3) alkylcarbonyl wherein X is chosen from N, O and S, or E is merely a bond;

and D may optionally be substituted with up to two groups chosen from OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy, N-heterocyclylacyl, C_1-C_3 alkylsulfonyl, sulfonamide and C_1-C_3 alkylsulfonamide;

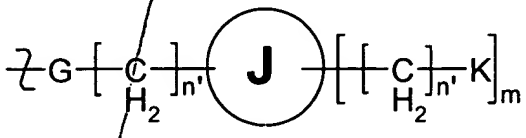
iii) C_1-C_6 alkanoyl; C_2-C-$_6$ alkenoyl; and methylthioC_1-C_5 alkanoyl, any of which may be substituted with up to two groups chosen from OH, C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy; C_1-C_6 alkyloxy; C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), amino, C_1-C_6 alkyl and phenyl amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters), carboxy(C_2-C_5)alkyloxy and N-heterocyclylacyl, C_1-C_3 alkylsulfonyl, sulfonamide and C_1-C_3 alkylsulfonamide;

and iv) a divalent group of the formula:



wherein each carbonyl of the divalent group bonds to the nitrogen to form a five-membered ring and Ra is as defined above;

B is selected from -OH; C_1-C_6 alkyl or C_1-C_6 alkyl amino, di(C_1-C_6 alkyl)amino, C_1-C_6 alkyloxy, N-heterocyclylic and



each n' is independently 0, 1 or 2;

m is 0, 1, 2 or 3;

and G is N or O;

J is selected from the group consisting of aryl having a 5 to 6 membered ring optionally including up to 2 heteroatoms selected from the N, O, and S; fused aryl rings of 8 to 14 atoms optionally including up to 3 heteroatoms selected from N, O, and S, mono or fused ring cycloalkyl having 5 to 12 carbon atoms, and mono or fused ring heterocyclic having 5 to 12 carbon atoms including up to 3 heteroatoms chosen from the group consisting of N, O, and S;

each K is chosen from OH, C_1-C_3 alkyl; C_1-C_6 alkylacylamino, C_1-C_6 alkylacyloxy, C_1-C_6 alkyloxy, C_1-C_6 alkylthioxy, amido (including primary, C_1-C_6 alkyl and phenyl secondary and tertiary), NH_2, mono and di(C_1-C_6 alkyl and phenyl) amino, carbamyl (including C_1-C_6 alkyl and phenyl amides and esters), carboxyl (including C_1-C_6 alkyl and phenyl esters) and carboxy(C_2-C_5)alkyloxy;

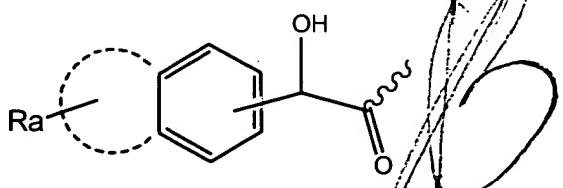
R1 is straight or branched chain C_1-C_5 alkanyl or C_2-C_5 alkenyl;

R2 is C_{1-5} straight or branched chain alkanyl or alkenyl; methylthiomethyl; aryl or arylalkyl or heteroaryl or heteroarylalkyl wherein any of the above are optionally substituted with up to 2 of C_{1-3} alkyl, trifluoromethyl or halogen,

and pharmaceutically acceptable salts and esters thereof and a pharmaceutically acceptable diluent.

B3

48) The composition claim 47 wherein A is:



wherein the dotted line indicates an optional aryl ring fused to the phenyl ring.